REMARKS

Upon entry of the present amendment, claims 1, 5-8, 10-13, 17-20, 22-24 and 78-85 are pending in the application. Claims 2-4 and 14-16 have been cancelled without prejudice or disclaimer. Claims 1, 6, 7, 13, 18 and 19 have been amended, and claims 78-85 have been added. The present amendments are fully supported by the specification and the claims as originally filed. For example, support for the amendments to independent claims 1 and 13, as amended herein, is found at least at page 18, lines 24-30; and at page 29, lines 8-9. Support for new claims 78-85 is found at least at page 13, lines 9-25. Claims 6, 7, 18 and 19 have been amended to maintain claim dependency in light of the cancellation of claims 3, 4, 15 and 16. Accordingly, no new matter has been added by this filing.

Rejections under 35 U.S.C. §102(e)

Claims 1-3, , 7-8, 10-15, 17, 19-20 and 22-24 been rejected under 35 U.S.C. § 102(e), as being anticipated by U.S. Patent No. 6,479,481 by Stendel *et al.* ("Stendel").

Claims 1 and 13 have been amended to recite methods of inhibiting growth of recurrent autologous tumors, wherein the tumor is ovarian cancer. Stendel, however, does not teach or suggest methods of treating any ovarian tumors. Accordingly, this reference fails to teach every element of the claimed invention. As such, the amended claims are novel over Stendel, and this rejection should be withdrawn.

Rejections under 35 U.S.C. § 103

Pfirrmann and Morrissey

Claims 1-2, 5, 10-14, 17-20 and 22-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,593,665 by Pfirrmann *et al.* ("Pfirrmann") in view of International Publication No. WO 98/52572 by Morrissey *et al.* ("Morrissey"). According to the Examiner, "it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the teachings of Pfirrmann on the use of taurolidine and taurultam in treating tumors, by adding the method of treatments as taught by Morrissey, because of the expectations of treating patients in need of such treatments with the most effective medications and the least possible amount of side effects." (Office Action, pages 4-5).

Independent claim 1 has been amended to recite a method of inhibiting growth of a recurrent autologous tumor in a mammal by administering to the mammal a composition

comprising taurolidine or a biologically active derivative thereof, in an amount sufficient to induce tumor cell death by apoptosis, wherein the tumor is ovarian cancer. Claim 13, as amended, is directed to a method of inhibiting growth of a recurrent autologous tumor in a mammal by administering to the mammal a composition comprising taurultam or a biologically active derivative thereof, in an amount sufficient to induce tumor cell death by apoptosis, wherein the tumor is ovarian cancer.

Applicants respectfully disagree with the Examiner's characterization of the teachings of the Pfirrmann reference. In particular, Applicants submit that this reference does not teach or suggest the use of taurolidine and taurultam alone in the treatment tumors. Rather, Pfirrmann only teaches the administration of taurolidine and/or taurultam in combination with TNF. There is no teaching of suggestion in this reference to administer taurolidine and/or taurultam in the absence of TNF to treat tumors. Moreover, Pfirrmann actually teaches away from using taurolidine and taurultam in methods of treating tumors by concluding that "the primary effect of taurolidine and taurultam is in reducing or eliminating the toxic side effects of TNF." (*See* Pfirrmann, col. 2, lines 22-24). Thus, Applicants submit that a person of ordinary skill in the art would not have been motivated by the teachings of Pfirrmann to administer taurolidine and taurultam in the absence of TNF.

To support the characterization of the Pfirrmann reference, the Examiner has cited a passage at column 1, lines 65-66 that indicates that "taurolidine and taurultam do not inhibit the antitumour effect of TNF but, in fact augment such cytotoxicity". There is no teaching or suggestion in Pfirrmann that this increased cytotoxicity is due to anti-tumor effects of the taurolidine and/or taurultam, rather than an increase in the anti-tumor efficacy of TNF itself (*i.e.*, TNF itself is more successful because it is better tolerated by subjects in the presence of taurolidine and/or taurultam). In fact, the passage immediately preceding the statement cited by the Examiner indicates that Pfirrmann believed that taurolidine and taurultam reduce the toxicity and side effects of TNF by interfering with the interaction between TNF and endotoxins or metabolic products derived from endotoxins. (*See* Pfirrmann, col. 1, lines 60-64). The passage cited by the Examiner is offered by Pfirrmann as evidence to support the mechanism of action of taurolidine and taurultam vis-à-vis TNF, not vis-à-vis the target tumor.

In addition, Pfirrmann fails to describe or suggest treatment of ovarian cancer. This reference does not describe or suggest any particular cancer type suitable for such treatment. In fact, one of skill in the art would not be motivated to use the therapeutic method of Pfirrmann

(taurolidine or taurultam together with TNF) to treat ovarian cancer, because TNF was known to be contraindicated for ovarian cancer. At the time of the invention, TNF was known to "be important to the early stages of epithelial tumor promotion", play a role in "promoting development of tumor stroma", and acting as a "fuel that fans the flame" of cancer. (*See* Ness *et al.*, JNCI, vol. 92:162-163 (2000), copy enclosed). Thus, the skilled artisan would not be motivated to administer TNF to an ovarian cancer patient.

Accordingly, Applicants submit that the methods recited by the amended claims are not rendered obvious by the teachings of the Pfirrmann reference. The addition of the Morrissey reference fails to cure the deficiencies in the teachings of Pfirrmann, as Morrissey does not teach or suggest the use of taurolidine and taurultam in the treatment of recurrent ovarian tumors. As acknowledged by the Examiner, the Morrissey reference describes the treatment of leukemia only. There is no teaching or suggestion that would motivate the skilled artisan to use taurolidine to treat other types of cancer, let alone recurrent ovarian tumors. Moreover, the teachings of the Morrissey reference, which relate to one specific type of cancer, would not provide the skilled artisan with a reasonable expectation that the use of taurolidine would successfully inhibit the growth of a recurrent ovarian tumor.

Thus, Pfirrmann and Morrissey, alone or in combination, do not disclose or suggest the use of taurolidine, taurultam and/or biological derivatives thereof to inhibit the growth of a recurrent ovarian tumor. Accordingly, Applicants submit that the amended claims presented herein are not rendered obvious by the Pfirrmann and Morrissey references. Withdrawal of this rejection is, therefore, requested.

Pfirrmann, Morrissey and Samid

Claims 3-4, 6-8 and 15-16 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Pfirrmann in view of Morrissey, and in further view of U.S Patent No. 5,661,179 by Samid ("Samid"). According to the Examiner, "it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the combined teachings of Pfirrmann and Morrissey by substituting phenylacetate of Samid with taurolidine and/or taurultam, with a reasonable expectation of successfully producing compositions and methods of treatment for various tumors." (Office Action, page 6).

As described above, the pending claims have been amended to recite methods of inhibiting recurrent ovarian tumors in a mammal using taurolidine, taurultam and/or biological derivatives thereof.

For all of the reasons set forth above, Pfirrmann and Morrissey, alone or in combination, do not disclose or suggest the use of taurolidine, taurultam and biological derivatives thereof to inhibit the growth of recurrent ovarian tumors. The teachings of Samid fail to remedy the deficiencies in the teachings of the Pfirrmann and Morrissey references, as Samid does not teach or suggest the use of any compounds to inhibit the growth of a recurrent ovarian tumor, let alone the use of taurolidine, taurultam and/or biological derivatives thereof in the treatment of recurrent ovarian tumors. Moreover, Applicants submit that the skilled artisan working with taurolidine and taurultam at the time the instant application was filed would have had no motivation to even look to the Samid reference, as taurolidine and taurultam do not contain phenylacetic acid or a phenylacetic acid derivative.

Thus, the Pfirrmann, Morrissey and Samid references, alone or in combination, do not render the methods recited by the amended claims obvious. As such, Applicants request that the Examiner withdraw this rejection.

Monson

Claims 1-8, 10-20, and 22-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over International Publication No. WO 92/00743 by Monson ("Monson""). According to the Examiner, "it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the Monson's teachings by branching off methods of treatment, prophylaxis and types of tumors such as glioblastomas and ovarian cancers." (Office Action, page 7).

As described above, the pending claims have been amended to recite methods of inhibiting recurrent ovarian tumors in a mammal using taurolidine, taurultam and/or biological derivatives thereof.

In contrast to the methods recited by the amended claims presented herein, Monson fails to describe or suggest any methods of treating any ovarian tumors, let alone recurrent ovarian tumors in a mammal using taurolidine, taurultam and/or biological derivatives thereof. Applicants respectfully disagree with the Examiner's characterization that a mere listing of tumors to be treated, such as lymphomas, sarcomas, melanomas and carcinomas, in the Monson

reference renders the claimed methods of inhibiting recurrent ovarian tumors obvious. Those of ordinary skill in the art will appreciate that numerous factors such as, *e.g.*, the etiologies, mechanisms of action, and effective treatments, vary from cancer type to cancer type. Thus, teachings directed to one type of cancer cannot automatically be applied in the treatment of other cancer types. Accordingly, the teachings of the Monson reference would not provide the skilled artisan with a reasonable expectation that the use of taurolidine and taurultam would successfully inhibit the growth of a recurrent ovarian tumor.

Applicants submit, therefore, that the amended claims presented herein are not rendered obvious by the Monson reference. As such, this rejection should be withdrawn.

Double Patenting Rejections

Claims 1, 8, 10-20 and 22-24 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,703,413 ("the '413 patent"). Claims 1-8, 10-20 and 22-24 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-43 of U.S. Patent No. 6,995,164 ("the '164 patent"). Claims 1-8, 10-20 and 22-24 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of co-pending U.S. Application No. 11/350,313 ("the '313 application").

Applicants will submit terminal disclaimers over the '413 patent, the '164 patent and the '313 application upon indication of allowable subject matter in the instant application.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact any of the undersigned at the telephone number provided below. The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-031 CON2.

Respectfully submitted,

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